January 26, 2006

Matthew Barmasse
EHSQ Director
ISOCHEM Inc.
1 North Transit Road
Lockport, NY 14094

Dear Mr. Barmasse:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for p-toluenesulfonyl isocyanate posted on the ChemRTK HPV Challenge Program Web site on July 21, 2004. I commend ISOCHEM Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that ISOCHEM advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: N. Patel
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
p-Toluenesulfonyl isocyanate (PTSI)

Summary of EPA Comments

The sponsor, ISOCHEM, Inc., submitted a test plan and robust summaries to EPA for p-toluenesulfonyl isocyanate (PTSI, CAS No. 4083-64-1) dated June 12, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on July 21, 2004. Information on a proposed analog, p-toluene-sulfonamide (PTSA, CAS # 70-55-3), was also included.

EPA has reviewed this submission and has reached the following conclusions:

1. Analog Justification. Data were provided for the hydrolysis product, PTSA, to satisfy most of the SIDS endpoints for PTSI. Although this approach is reasonable the submitter needs to support this rationale with measured sulfonyl isocyanate hydrolysis half-life data to confirm and better define "rapid" hydrolysis.

2. Physicochemical Properties. The submitter needs to provide additional vapor pressure data for the sponsored substance.

3. Environmental Fate. The submitter needs to provide measured ready biodegradation data for PTSA and more information on stability in water.

4. Health Effects. EPA reserves judgement on adequacy of PTSA data pending the submission of measured hydrolysis rate data. Then the submitter needs to address deficiencies in the PTSA robust summaries.

5. Ecological Effects. EPA agrees that it is reasonable to use data for the hydrolysis product, PTSA. However, the submitter needs to add the available measured data to the submission.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the p-Toluenesulfonyl Isocyanate Challenge Submission

Analog Justification

The submitter states that PTSI will hydrolyze rapidly to the corresponding carbamic acid followed by rapid decomposition to carbon dioxide and PTSA. The submitter proposes using data for PTSA to satisfy the SIDS endpoints for PTSI.

EPA considers this rationale generally reasonable. However, particularly for health effects evaluation, the submitter needs to support the approach by providing a measured hydrolysis half-life for PTSI or by submitting corresponding data for an appropriate analog(s) (see Environmental Fate section below).

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for melting point, boiling point, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

Vapor pressure. The vapor pressure value provided by the submitter is not adequate for the purposes of the HPV Challenge Program. The submitter provided a single measured value of 1 mm Hg at 100 ºC for PTSI. According to the HPV Challenge guidance, vapor pressure needs to be reported at 25 ºC. Although extrapolated values from a series of measurements at elevated temperatures are acceptable in lieu of a measurement at 25 ºC, a single measured high-temperature value is not adequate to address this endpoint. Therefore, the submitter needs to provide a measured vapor pressure value at 25 ºC following OECD TG 104, or extrapolate a value from a series of measurements at elevated temperatures.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for photodegradation and fugacity are adequate for the purposes of the HPV Challenge Program.

Stability in water. The submitter stated that PTSI hydrolyzes rapidly to the corresponding carbamic acid followed by rapid decomposition forming carbon dioxide and PTSA. This assertion is reasonable. However, the submitter needs to support this rationale by providing a measured hydrolysis half-life for PTSI or by providing corresponding data for one or more analogous sulfonyl isocyanates, with technical discussion as appropriate.

Biodegradation. The submitted data are not adequate for the purposes of the HPV Challenge Program because the test method used by the submitter relies on a single type of bacteria as inoculum (*Pseudomonas* sp.). The submitter needs to provide measured ready biodegradation data for PTSA, the hydrolysis product of PTSI, following OECD TG 301.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

With the exception of an acute toxicity value for PTSI, data for PTSA were submitted for the other health effects endpoints. The submitted PTSI data for acute toxicity are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of the PTSA data for genetic, repeated-dose, reproductive and developmental toxicity until the hydrolysis issue is clarified (see above). When that occurs, the submitter will need to address deficiencies in the robust summaries because several important details are missing from the robust summaries for the screening test for repeated-dose/reproductive/ developmental toxicity (OECD TG 422), such as histopathology and information on parameters for assessing developmental toxicity. The submitter needs to consult the HPV guidance document for preparing robust summaries.

Ecological Effects (fish, invertebrates, and algae)

The submitter provided estimated data on PTSA for all endpoints. Although EPA agrees that it is reasonable to use data for the hydrolysis product PTSA, the submitter needs to include the measured PTSA data available on the UNEP website (http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html rather than the estimated values. Because the published OECD data for these effects predate the current data summary standards, the summaries need to be made robust for the purposes of the HPV Challenge Program. More study details may be available through the OECD SIDS contact for Japan:

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Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. The robust summary is missing the following information: species used, number of animals, route of exposure, doses used, organs evaluated at necropsy and the results of the evaluation.

Repeated Dose/Developmental and Reproductive Effects. Information is needed as to the rationale for the selection of doses and use of vehicle. Specific information is needed on changes in body weight, food and water consumption, body weight at sacrifice, organ weight data, results and identification of tissues examined for histopathology, length of gestation, number of live births and post implantation loss, number of runts, number of implantations, corpora lutea (recommended), litter size and weights, time of death during the study and statistical treatment of the results.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.